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Does an Adjuvant AV-fistula Improve the Patency of a Femorocrural PTFE bypass with Distal Vein Cuff in Critical Leg Ischaemia?—A Prospective Randomised Multicentre Trial

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Introduction. *A lack of suitable veins can cause serious problems when attempting to revascularise critically ischaemic legs. Prosthetic grafts have much worse patency in the femocrural position, despite the use of distal anastomotic cuffs. The use of adjuvant AV-fistula at the distal anastomosis should increase the graft flow above the thrombotic threshold velocity and thus increase prosthetic graft patency.*
Aim. *The aim of the study was to evaluate the benefit of an adjuvant AV-fistula on the patency of a femorocrural PTFE bypass with a distal vein cuff.*
Materials and methods. *This prospective randomised multicentre trial was conducted in four centres. A total of 59 patients with critical leg ischaemia and no suitable veins for grafting were randomised to receive a femocrural PTFE bypass and distal vein cuff, with or without an adjuvant AV-fistula. Thirty-one patients were randomised to the AV-fistula group (AVFG) and 28 to the control group (CG). Six patients were lost to follow-up during the 2-year study time.*
Results. *There were six immediate occlusions in each treatment group, but half of these were saved by re-operation. The mean postoperative ankle-bachial index (ABI) was 0.85 in the AVFG and 0.94 in the CG. The primary and secondary patency rate at 2 years was 29 and 40% for the AVFG and 36 and 40% for the CG (NS). Leg salvage at 2 years was 65 and 68%, respectively (NS).*
Conclusion. *Adjuvant AV-fistula does not improve the patency of a femorocrural PTFE bypass with a distal vein cuff.*

Key Words: Critical leg ischaemia; Femorocrural bypass; Distal vein cuff; Adjuvant AV-fistula; Patency; Outcome.

Introduction

Prosthetic bypass may be an alternative to primary amputation for limb salvage in patients with critical leg ischaemia and no suitable autologous vein.[1–6] However, the patency of prosthetic bypass is inferior to that of vein. Vein cuff interposition has been reported to be beneficial in femorocrural PTFE reconstructions.[7–11] The patency is, however, often threatened by a limited outflow. Sauvage first hypothesised the thrombotic threshold velocity (TTV), a velocity below which thrombosis occurs.[12] Vein cuffs may reduce the mismatch in compliance between the recipient artery and the prosthetic graft and alter the flow characteristics at the anastomosis, thus reducing myointimal hyperplasia. However, they do not improve graft flow. An adjuvant AV-fistula may elevate the flow velocity above the thrombotic threshold. It has been previously postulated that an adjuvant AV-fistula might have a beneficial effect on the patency of a femorocrural PTFE bypass by increasing blood flow above the thrombotic threshold.

This Scandinavian multicentre pilot trial was undertaken to compare 6 mm PTFE graft with distal vein cuff and adjuvant AV-fistula with similar graft without a fistula. The aim was to determine whether an adjuvant AV-fistula improved the 2-year outcome and if so, how large a patient sample would be needed to prove its superiority.

Materials and Method

Patients

This was a prospective randomised study that was carried out during the years 1997–2002 in four

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Scandinavian centres (Table 1). Fifty-nine patients were recruited and randomised between February 1997 and May 2000 according to a block randomisation stratified by the centre. The inclusion criteria were patients with critical leg ischaemia (rest pain, ulcers or gangrene) requiring femorocrural bypass, without a suitable vein for grafting. Patients were excluded from the study if they had only claudication, or if the bypass was to the popliteal or pedal artery.

The average age of the patients was 73.7 years (range 46–93 years). Fifty-eight percent of the patients were females. Forty-one percent had diabetes and 61% coronary artery disease (Table 2). Forty (68%) patients had distal ischaemic lesions with mean ABI of 0.30 and 0.36, respectively (Table 3). Seventy-one percent of the patients had had previous vascular surgery and in 34 (58%) cases the prosthetic bypass was a redo-procedure.

The haemodynamic severity of the ischaemia was assessed using Doppler ankle/brachial pressure index (ABI) and the morphology of the obliterative disease was assessed by digital subtraction angiography. The run-off score was evaluated preoperatively by the standards proposed by the Ad Hoc.[13] The run-off was evaluated both for the recipient crural artery and for pedal arch. Eight patients had inadequate angiographic data that did not allow outflow scoring.

Surgical procedure

There were 39 patients on antiplatelet and six on anticoagulation therapy preoperatively. All patients were heparinized during operation. All patients received oral antiplatelet therapy (ASA) postoperatively unless contraindicated, or the patients were already on anticoagulants for concomitant disease. Antibiotic prophylaxis of both vancomycin and cefuroxime or the latter alone was given to all patients. The surgical procedure was carried out with a 6 mm externally supported PTFE prosthesis (Gore or Impra Corp). An interposition vein cuff of the Miller type[14] (33), St Mary's Boot[15] (19) or a modified Miller type (7) was constructed at the distal anastomosis. Patients randomised to the AVFG received an AV-fistula of the common ostium type in 25 cases and the proximal type in six cases according to the surgeon's discretion. Any surgeon with previous experience of three AV-fistulas or more was accepted as an operator.

Table 2. Clinical data of the patients as related to the treatment group.

Clinical characteristic	AVF group	Control group
Age: mean, (range)	74.3 (49–93)	73 (46–88)
Sex: male/female	15/16	10/18
Diabetes	12 (39%)	12 (43%)
Hypertension*	15 (48%)	14 (50%)
Coronary artery disease	22 (71%)	14 (50%)
Cerebrovascular disease	6 (19%)	8 (29%)
Pulmonary disease	6 (19%)	2 (7%)
Renal failure†	2 (6%)	2 (7%)
Smoking	9 (29%)	12 (43%)

*Blood pressure >160/95 mmHg or medication.
†Level of serum creatinine >150 μmol/l.

Follow-up and statistics

The follow-up time was 2 years. Clinical examination and vascular laboratory visits took place at 7 days, 1, 3, 6, 9, 12, 18 and 24 months postoperatively. A sustained ABI increase of >0.15 was accepted as an indication of patency. When in doubt, a duplex scan was performed to assess patency. Routine duplex evaluation took place at the one-year follow-up visit. Clinical status, patency and complications were registered.

Primary and secondary patency, leg salvage and patients alive with a leg were calculated by the Life Table method and the Log-Rank test was used to compare the two groups. The dependency of graft patency on the patency of the fistula was analysed at one year by Fisher's exact test. The study protocol was approved by the local ethics committees.

Results

Thirty-one patents were randomised to the AV-fistula group (AVFG) and 28 to the control group (CG). The two treatment groups were comparable in terms of

Table 1. Centrewise distribution of the patients and severity of their diseases.

Centre	No. of patients	Mean ABI	Run-off AVF group	Run-off control group
Helsinki	37	0.37	7.25 (2–10)	5 (2–8.5)
Lappeenranta	13	0.34	6 (3–9)	5.5 (4–7)
Västerås	8	0.11	5.5 (1–5.5)	5.25 (1–6)
Hillerod	1	0.43	1	–
Total	59	0.33	6 (1–10)	5 (1–8.5)

ABI (mean) and run-off (median, range, scale 1–10). AVF group, group with adjuvant AV-fistula; control group, group without adjuvant AV-fistula.

Table 3. Indication for surgery, outflow vessel and preoperative ABI in AVF- and control group.

Indication	AVF group	Control group
Rest pain	8	11
Ulcers	16	14
Gangrene	7	3
A.tibilalis anterior	13	13
A.tibialis posterior	8	7
A.fibularis	10	8
ABI (mean)*	0.30	0.36

*Two patients with erroneous pressure readings due to media-sclerosis were excluded.

Table 5. Immediate complications in AVF- and control group.

Complication	AVF group	Control group	Total
Wound problem			12
Superficial infection	6	4	10
Lymph leakage	2	–	2
Compartment syndrome	1	1	2
Graft infection	1	–	1
General complication			9
Prolonged intensive care	1	1	2
Heart insufficiency	2	2	4
Pneumonia	–	1	1
Pulmonary embolism	1	–	1
Deep vein thrombosis	–	1	1

their demographics, as well as the indications for surgery, the outflow artery and preoperative ABI values.

There were no perioperative deaths. There were 12 (20%) immediate graft occlusions (<30 days), six in the AVFG and six in the CG. Nine of these underwent re-operation, which was successful in six grafts but three required amputation. Of the three non-reoperated patients, direct amputation was chosen in one case during the immediate post-operative period. In two cases conservative treatment was chosen leading to amputation at 9 months in one case and leg salvage at 2 years in the other case. In one case amputation required with a patent graft due to severe foot gangrene. The median ABI increase from the preoperative level was 0.55 in the fistula group and 0.57 in the control group at 1 month (Table 4). The median duration of the operation was 222 min in the AVFG and 179.5 min in the CG ($p = 0.04$).

Immediate postoperative complications were encountered in 24 patients, half of which were wound problems. Nine patients had general complications and all recovered (Table 5). Two superficial wound infections required revision of the wound, which led to healing of the infection and the others were treated conservatively. There were two compartment syndromes treated by fasciotomy following surgery. There was one immediate graft infection, which was cured by revision and a sartorius muscle flap, but the patient died of a myocardial infarction at 6 weeks.

There were six withdrawals during the 2-year surveillance. One drop out was at 3 months with a patent graft. One patient had an occluded graft at 15 months with no later record. Four patients were followed up to 18 months at which time two of the grafts were patent and two occluded. Ten percent (17%) patients died during the study. In six cases where the cause of death was known, it was not directly related to the surgery.

Table 4. Immediate results of the AVF- and control group.

	AVF group	Control group
Deaths	–	–
Occlusions	6	6
Re-operations	5	4
Amputations	2	3
ABI increase (mean)*	0.55	0.57

*Four patients with erroneous pressure readings due to media-sclerosis were excluded.

There were 24 late graft occlusions. In 13 cases re-operation was attempted. Secondary patency was achieved in three cases with thrombectomy and graft revision and in three cases the graft occluded despite additional procedures. Seven cases required a redo-procedure. The cumulative primary and secondary patencies were 29 and 40% in the AVFG and 36 and 40% in the CG. The primary and secondary patencies were similar ($p = 0.77$ and 0.89), irrespective of the presence or absence of the fistula (Figs. 1 and 2).

There were 13 amputations after the initial 30-day period, eight in the AVFG and five in the CG. Below-knee amputation was performed in four cases and above-knee in nine cases. Leg salvage and patients alive with a leg at 2 years were not affected by the operative technique chosen (Figs. 3 and 4, $p = 0.97$ and 0.60).

Late complications were encountered in four patients. One patient had a superficial wound infection at 3 months, which resolved. There was one late graft infection following thrombosis of the graft. The infection led to removal of the prosthesis and crural amputation at 9 months. The patient died at 10 months from myocardial infarction. One patient developed a MRSA-infection following occlusion and a redo-procedure. In another redo-procedure, cuff disruption was successfully treated by direct suture. One patient developed venous hypertension: oedema and static eczema related to the AV-fistula. The symptoms resolved after closure of the fistula at 3 months. The graft remained patent after the additional procedure.

Nineteen patients with AV-fistula were available for

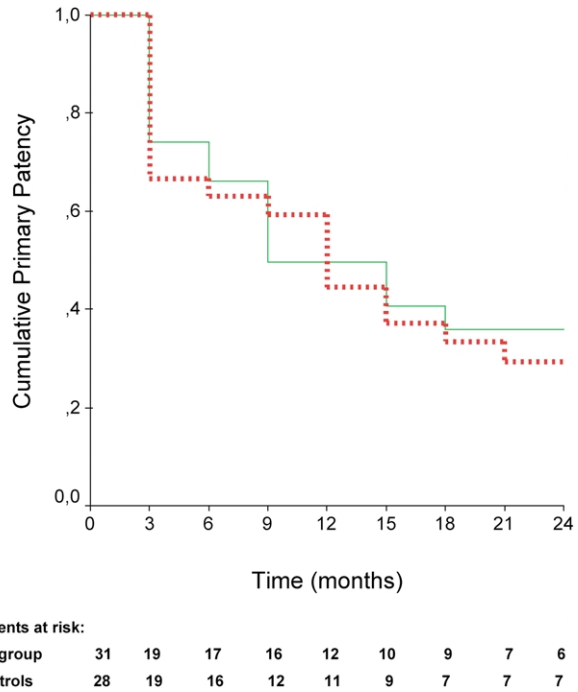

Fig. 1. Primary patency in subgroups of patients with femorocrural PTFE bypasses with AV-fistulas = AVF group (…) and without AV-fistulas = control group (—).

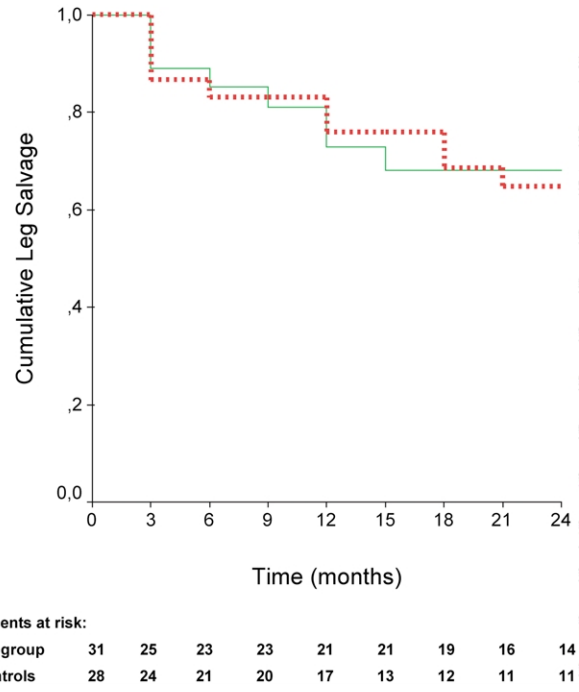

Fig. 3. Leg salvage in subgroups of patients with femorocrural PTFE bypasses with AV-fistula (…) and without AV-fistula (—).

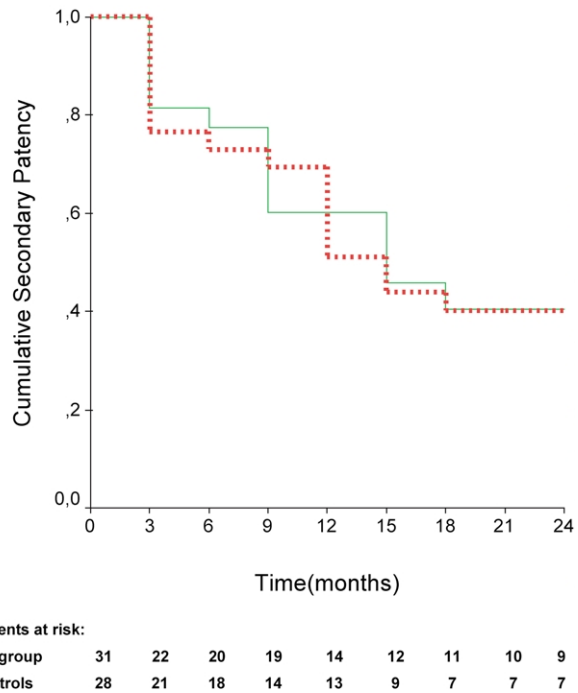

Fig. 2. Secondary patency in subgroups of patients with femorocrural PTFE bypasses with AV-fistulas (…) and without AV-fistulas (—).

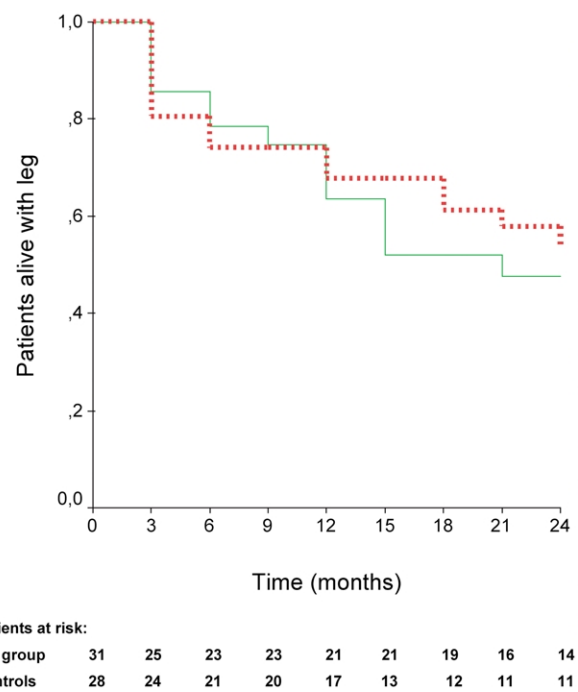

Fig. 4. Patients alive with leg in subgroups of patients with femorocrural PTFE bypasses with AV-fistula (…) and without AV-fistula (—).

duplex evaluation at 1 year. Out of the original 31 AVFG, four were amputated, three dead, three had occluded grafts and two patients were not available for surveillance. In all other cases, the patency of the AV-fistula was confirmed. In six cases, there was an occlusion of the AV-fistula and in only one case did this result in graft thrombosis, which after re-operation led to leg salvage. In one case where the fistula occluded a revision was done for threatened graft failure and this also resulted in leg salvage. There were five patients who had a record of a previously patent AV-fistula but had graft failure at 1 year. Two of these patients were re-operated and in three the occlusion led to amputation. This fistula patency data indicates that the patency of the graft is not dependent on the patency of the fistula ($p = 0.02$).

Discussion

The results of previous series of femorocrural prosthetic bypasses are difficult to compare to our results. Most studies are retrospective case series without controls, different adjunctive methods, different types of patient groups and different prostheses. Dardik *et al*. reported a series of 281 patients with femorocrural bypasses operated between 1979 and 1995 with a 3-year secondary patency rate of 61% and limb salvage of 74% using human umbilical vein and an adjunctive AV-fistula.[16,17] Jacobs has reported patency rates of 64–71% at one year and leg salvage rates of 72% with a PTFE bypass and an AV-fistula.[18,19] Kreienberg compared AV-fistula with vein cuff in below knee popliteal and tibial bypasses and found patency rates of 48 and 38%, respectively.[20] Vein cuff seemed to give better limb salvage rates than AV-fistula (92% vs 76% at three years). Moody *et al*. reported a patency rate of 39% at two years with human umbilical vein plus an AV-fistula and Eagleton *et al*. found no statistical difference between direct prosthetic anastomosis, vein cuff and AV-fistula (patency rates of 35–65% and limb salvage of 56–76% in femoro-infrapopliteal bypasses).[21,22] Harris *et al*. suggested an improved outcome with the combined use of an AV-fistula and a vein cuff.[23] Yet the only previous controlled trial where an AV-fistula was combined with a vein cuff is from Hamsho *et al*. They reported primary patency rates of 55 and 53% in both groups and leg salvage rates of 43–54% at one year.[24] Our results are in accordance with these results. The relatively small number of patients in this study risks a type two error. However, even if a larger study showed a statistical difference, it would not be clinically relevant.

Our results emphasise that early graft revision yields better secondary patency than late re-operations as a redo-procedure was often required after late graft revision. Only half of the late graft occlusions resulted in re-operation in our series. This shows that these patients may tolerate graft failure even though the indication was critical ischaemia. This is a well-known phenomenon especially in legs with healed skin lesions. Furthermore critical ischaemia does not inevitably lead to amputation.[25] The effect of re-operation on patency is clear as shown by the difference between primary and secondary patency and, therefore, the role of re-operation must be emphasised.

If the AV-fistula is constructed to achieve flow above TTV, it can be postulated that the occlusion of an adjuvant AV-fistula would result in graft thrombosis. In our series, a large proportion of grafts stayed open despite the occlusion of the fistula. This finding emphasises the lack of benefit on prosthetic graft patency.

High output cardiac failure, venous hypertension and steal effect are described as possible complications of an AV-fistula. In our study we only had one patient with symptoms of venous hypertension. In our previous experience, we have had one patient with cardiac failure due to an adjuvant AV-fistula.[26] In this case the cardiac overload was caused by a too large fistula with a flow of 1000 cm/s. We did not encounter steal effects in these patients as they all had uncompromised inflow. The ABI increase in both groups was similar also indicating that in fact the AV-fistula did not cause a steal effect from the distal circulation. A substantial increase in the ABI for both groups reflected the improved distal circulation.[18]

In summary, an AV-fistula does not improve the patency of PTFE femorocrural bypass grafts with a distal interposition vein cuff. Furthermore, it increases the operation time and the technical challenge.

Appendix

ScanPAC Study Group (Scandinavian Prosthesis, AV-fistula and Cuff Study).

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